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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,759	07/17/2003	Manfred Galle	029300.52497US	9152

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,759	GALLE ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on March 10, 2005 has been received and entered into the case. Claims 1 – 18 are pending, claims 14 – 18 are withdrawn from consideration; claims 1 – 13 have been considered on the merits. All arguments have been considered.

Election/Restrictions

Applicant continues to traverse the election restriction requirement. Applicant continues to argue that the composition cannot be used for any other method, and the method requires the instant composition. However as stated before, other materially different products could be used to treat maldigestion such as lactobacillus. In addition, the instant composition could be used in other methods such as for treating foodstuff waste products, cleaning compositions, or dry cleaning compositions.

It is noted that the election/restriction was made FINAL in the previous office action.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1 – 13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sipos in view of Ogawa.

Applicant claims a composition comprising a concentrated lipase of Phizopus delemar, a neutral protease of Aspergillus mellus, and an amylase of Aspergillus oryae. The lipase has a specific activity of 1,800,000 FIP units/gram; the protease has a specific activity of 7,500 FIP units/gram; and the protease has a pH optimum of 6 – 8. Applicant claims a pharmaceutical composition comprising the enzyme mixture and at least one carrier or adjuvant. The composition is in a form selected from a powder, pellets, microspheres, capsules, sachets, tablets, liquid suspension or liquid solution; at least one of the enzymes are individually pelleted; or is film coated with an enteric layer. Specifically the protease is pelleted and film coated with an enteric layer; the lipase is pelleted and film coated; or alternatively the protease and lipase are pelleted and film coated. The compositions comprises the lipase : amylase : protease ratio at 50 – 500FIP lipase : 40 – 120 FIP amylase : 1 FIP protease; and each dose contains at least 10,000 FIP units lipase, 8000 FIP units amylase and 200 FIP units protease.

Sipos teaches pharmaceutical compositions for treating digestive disorders comprising protease, lipase (3.1.1.3, lipase of Rhizopus delemar) and amylase (3.2.1.1, amylase of Aspergillus oryzae) (col.6 line 11-21). The compositions and ingredients are formed into microspheres or microtablets, contain suitable carriers and/or adjuvants (examples), and are individually coated with an enteric coating (col.5 line 62-67, col.7 line 21-30). Sipos teaches the compositions are buffered to provide an optimum pH of 7 – 10 (col.6 line 50-51).

Sipos does not teach the compositions wherein the protease is a neutral protease of Aspergillu melleus, wherein its optimum pH is 6 - 8. However, Ogawa teaches compositions for treating digestive disorders comprising the digestive protease Prozyme 6 (neutral protease of Aspergillus melleus) (abstract, col.4 line 1-29). As evidenced by Ogawa, neutral protease of Aspergillus melleus was a well-known and used protease in the art for compositions that treat digestive disorders. At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use neutral protease of Aspergillus melleus as the protease in the composition of Sipos, since it was well-known and used for its claimed purpose, as evidenced by Ogawa. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Ogawa to use neutral protease of Aspergillus melleus as the protease in the composition of Sipos, with a reasonable expectation for successfully obtaining an effective composition for treating digestive disorders. Although the references do not specifically teach that the protease has an optimum pH of 6 – 8, the protease of Ogawa is the same as the claimed protease. Therefore, the protease of Ogawa must also have the same characteristics of the claimed protease, specifically an optimum pH of 6 – 8.

Sipos does not teach the composition wherein the lipase and protease have the claimed specific activities, or wherein the composition comprises the claimed ratios or amounts of enzymes. However, Sipos does teach the compositions with varying activities of lipase, amylase and protease. Specifically 4000 – 8000 USP lipase; 25,000 – 40,000 USP amylase; and 25,000 – 45,000 USP protease (examples 2,3). Sipos further teaches the compositions comprising 10 – 70% enzymes with varying amounts of each enzyme (examples) and that the amounts and dosages are variable and can be optimized according to the condition, patient and practitioner (col.15 line 39-48). In addition, Ogawa teaches the compositions comprise amounts of protease sufficient to exert digestive activity; specifically at least 200 FIP units or 15,000 units (col.4 line 32-56) and that the compositions can be changed and/or modified by one of ordinary skill in the art (col.13 line 7-11).

It is well known in the art that enzyme activity is determined by the quantity of substrate transformed or product formed per unit of time (International Commission of Pharmaceutical Enzymes F.I.P). Since such activities are dependent on a number of experimental conditions (pH, temperature, presence of inhibitors/activators), one of ordinary skill in the art would know to optimize such conditions to attain a desired activity. As evidenced by Sipos and Ogawa, the specific activities of the instant enzymes in compositions for treating digestive disorders were routinely variable. As such, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize specific activities, dosages and amounts of each enzyme as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Sipos, Ogawa and standard practice, to optimize the specific activities, amounts and ratios of the instant

enzymes with a reasonable expectation for successfully obtaining a composition effective for treating digestive disorders.

Response to Arguments

Applicant argues that there is no teaching to combine the instant references; that the references do not teach all of the claimed limitations; that the enzymes of Sipos merely use the same nomenclature as the claimed enzymes; that the art prefers animal enzymes to the claimed sources; tand hat Sipos requires 15 – 60% buffer, which reduces amount of enzymes and therefore has lower activity. Applicant additionally argues that Ogawa is not analogous to Sipos, since the composition of Ogawa is used for a different purpose; and that Ogawa does not teach the use and method as applicant. Finally, applicant argues that it would not be routine to interchange enzymes in compositions, even though they may exhibit similar activities.

However, these arguments fail to persuade because as stated above, one of ordinary skill in the art would have been motivated to combine the instant enzymes together because Sipos teaches combining a lipase, protease and amylase in compositions for treating digestive disorders. While Sipos does not teach the exact source of enzymes, they are clearly identified as the same as applicant. Applicant identifies the same enzymes throughout the specification as the preferred enzymes. Specifically, that the enzymes are those disclosed in the prior art (spec, pages 7, 9 – 11). Since the references teach the same enzymes for the same purpose, it would have been obvious to one of ordinary skill in the art to combine the instant enzymes in a composition with a reasonable expectation for successfully obtaining an effective composition

for treating digestive disorders. Particularly absent evidence of unexpected results, benefits, or advantages of the claimed composition.

Regarding applicant's arguments that the art requires more buffer, this argument is not commensurate in scope with the claims. The rejected claims do not require a particular amount of buffer, and do not exclude any amount of buffer, as they are open-ended. Thus any amount of buffer may be included in the claimed composition. It is reiterated that applicant uses the same enzymes for the same purpose as disclosed by the cited references, thus absent unexpected results or benefits, the claims are rendered obvious.

Regarding applicant's assertion that Ogawa is non-analogous to Sipos, it is noted that Ogawa specifically teaches digestive enzymes in compositions for treating digestive disorders, as does Sipos. Therefore the references are considered analogous. In reference to applicant's arguments that Ogawa does not teach the method of applicant, the claims are directed to a composition, not a method, therefore this argument is not commensurate in scope with the claims.

Finally, regarding applicant's assertion that it is not routine to interchange enzymes, the references clearly teach the same enzymes (albeit from different sources), for the same purpose as argued by applicant. Therefore, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the instant enzymes for their known purpose and use, with a reasonable expectation for successfully obtaining a composition effective for treating maldigestion and/or digestive disorders. Therefore, the claims stand rejected.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 571-272-0915. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ruth A. Davis
May 27, 2005
AU 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER